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Full length article

Protective glove use and hygiene habits modify the associations of specific pesticides with Parkinson's disease



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ARTICLE INFO

Article history:
Received 17 July 2014
Received in revised form 12 October 2014
Accepted 6 November 2014
Available online 21 November 2014

Keywords:
Personal protective equipment
Parkinson's disease
Pesticides
Neurodegenerative diseases
Movement disorders

ABSTRACT

Pesticides have been associated with Parkinson's disease (PD), and protective gloves and workplace hygiene can reduce pesticide exposure. We assessed whether use of gloves and workplace hygiene modified associations between pesticides and PD. The Farming and Movement Evaluation (FAME) study is a nested case–control study within the Agricultural Health Study. Use of protective gloves, other PPE, and hygiene practices were determined by questionnaire (69 cases and 237 controls were included). We considered interactions of gloves and hygiene with ever-use of pesticides for all pesticides with ≥ 5 exposed and unexposed cases and controls in each glove-use stratum (paraquat, permethrin, rotenone, and trifluralin). 61% of respondents consistently used protective gloves and 87% consistently used ≥ 2 hygiene practices. Protective glove use modified the associations of paraquat and permethrin with PD: neither pesticide was associated with PD among protective glove users, while both pesticides were associated with PD among non-users (paraquat OR 3.9 [95% CI 1.3, 11.7], interaction p = 0.15; permethrin OR 4.3 [95% CI 1.2, 15.6] interaction p = 0.05). Rotenone was associated with PD regardless of glove use. Trifluralin was associated with PD among participants who used < 2 hygiene practices (OR 5.5 [95% CI 1.1, 27.1]) but was not associated with PD among participants who used < 2 or more practices (interaction p = 0.02). Although sample size was limited in the FAME study, protective glove use and hygiene practices appeared to be important modifiers of the association between pesticides and PD and may reduce risk of PD associated with certain pesticides.

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1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the United States. Approximately 1% of the population over age 60 and 4% over 80 are affected in industrial nations (de Lau and

Abbreviations: AHS, Agricultural Health Study; FAME, Farming and Movement Evaluation; NIEHS, National Institute of Environmental Health Sciences; PPE, personal protective equipment; PD, Parkinson's disease; OR, odds ratio; Cl, confidence interval.

* Corresponding author at: Box 7435, University of North Carolina, Gillings School of Global Public Health, Department of Epidemiology, Chapel Hill NC 27599, United States. E-mail address: furlongm@med.unc.edu (M. Furlong). Breteler, 2006). Pesticide exposure has been associated with PD in some epidemiological studies and with parkinsonian symptoms in animal studies (Betarbet et al., 2000; Brown et al., 2006; Pezzoli and Cereda, 2013; Priyadarshi et al., 2000). Specifically, the pesticide paraquat has been associated with PD in multiple epidemiological studies (Costello et al., 2009; Kamel et al., 2007; Liou et al., 1997; Tanner et al., 2011), whereas associations between PD and rotenone (Tanner et al., 2011), permethrin (Tanner et al., 2009), and trifluralin (Kamel et al., 2007) have been less frequently reported. Numbers of exposed cases in these studies are small (see Tanner et al., 2011), limiting the ability to assess possible modifying factors.

Personal protective equipment (PPE) may protect workers from exposure to pesticides. In agricultural field studies, PPE use has been associated with reduced biomarkers of exposure (López et al., 2007; Quandt et al., 2006), although gloves worn during pesticide application may also serve as a reservoir of those pesticides during future use (Hines et al., 2001). Still, in the Agricultural Health Study (AHS), chemically-resistant gloves appear to provide the greatest reductions in exposure compared to other types of PPE, and AHS models predict that farmers would reduce exposure by up to 90% by wearing gloves in conjunction with several other types of PPE (Hines et al., 2011; Thomas et al., 2009).

Occupational hygiene practices may also be important in reducing exposure to pesticides (Salvatore et al., 2008). Immediately washing hands after pesticide use may reduce exposure to pesticides, with removal efficiency varying by time elapsed since exposure and specific pesticide characteristics (Fenske and Lu, 1994; Fenske et al., 1998). Immediately changing clothes that were worn during mixing and applying may also reduce exposure (Grieshop et al., 1994; van Balen et al., 2011). Together, PPE and hygiene practices may account for a significant amount of variability in studies that examine the association between pesticides and PD, yet no occupational studies of pesticides and PD have evaluated these practices. Such practices, however, have been associated with reduced risk of cancer associated with pesticide exposure (Zahm et al., 1990).

Stratifying pesticide use by PPE and hygiene practices may help identify individuals with more or less exposure. For example, farmers who apply paraquat without wearing any PPE may be exposed to a greater amount of paraquat than those who apply it while wearing gloves and full body coveralls, assuming similar application and mixing methods. Thus, in the absence of measured levels of exposure, analyzing the modifying effects of PPE and hygiene may provide indirect evidence of a dose–response relationship between specific pesticides and PD and also provide information on the health benefit of employing these practices when using pesticides.

2. Methods

2.1. Study population and questionnaires

The Farming and Movement Evaluation (FAME) study is a case-control study nested within the Agricultural Health Study (AHS), a prospective cohort study including 52,394 private pesticide applicators, mostly farmers, and 32,345 of their spouses, recruited from 1993 to 1997 in Iowa and North Carolina (Tanner et al., 2011). Suspect prevalent PD cases in the AHS were identified by self-report or from state mortality files. Potential controls randomly selected from the AHS cohort were frequency-matched to cases by age at enrollment into the AHS (<40, $40-49, 50-59, 60-64, 65-69, \ge 70$ years), sex, and state at a ratio of approximately three controls per case. During home visits, neurologists examined living suspect cases and 5% of controls, and neurologisttrained technicians examined the remaining controls to ensure they did not have PD. Controls with evidence of parkinsonism had a second in-home examination by a neurologist. Case status was determined by agreement of two movement disorder specialists following established criteria for PD (Gelb et al., 1999) and using information from medical records, the in-home examination, and a videotaped movement evaluation conducted during the home visit. Diagnosis dates were determined from medical histories collected during in-home exams and from medical records. Proxy informants were used for subjects that were unable to complete interviews (n = 16; 14 cases and 2 controls).

Cases and controls in FAME completed structured telephone interviews between 2002 and 2008 that collected information on demographics, lifestyle, medical history, a complete occupational history including details of all farm jobs, and information on PPE and hygiene practices.

2.2. Exposure assessment

2.2.1. Pesticides

The complete occupational history was used to evaluate exposure to 31 different pesticides (for a full list see Tanner et al. (2011)) in each job held between age 14 and a reference date. The reference date for cases was age at PD diagnosis while, for controls, it was the median age of PD diagnosis for cases in the corresponding age-, sex-and state-specific stratum. The 31 pesticides were chosen based on possible mechanistic links with PD and do not necessarily include those in common use. Pesticides that were banned, had their registrations canceled, or were voluntarily pulled from the market before 1985 (aldrin, DDT, and dieldrin) were not considered, since the PPE survey only evaluated the period after 1985 (see Section 2.2.2).

2.2.2. Personal protective equipment and hygiene practices

To reduce bias associated with lengthy historical recall and capture a time period before PD onset for most cases, the PPE questions focused on practices during the late 1980s and early 1990s; therefore, only individuals who used pesticides during this period were asked these questions. Of the 498 FAME subjects, 306 (237 controls, 69 cases) reported personally mixing or applying pesticides during the relevant period and completed the PPE survey; both licensed applicators and their spouses who used pesticides (but were not necessarily licensed) and responded to the PPE survey were included.

The survey included questions on use of gloves and other types of PPE more than half the time while mixing or applying pesticides (<50% gloves vs $\ge50\%$ gloves; <50% other PPE vs $\ge50\%$ other PPE) and on occupational hygiene practices. PPE and hygiene practices were not asked in relation to specific pesticides but rather were reported as general habits (PPE survey questions are in Appendix A1).

Protective gloves included chemically resistant gloves and plastic or rubber gloves, if indicated in the "other" category of glove use. Use of leather or fabric gloves was classified as "no protective glove use," as such materials provide little to no protection against solvents and chemicals (Frank, 1994). These glove categorizations have been used in previous research on pesticide exposure reduction assessments [reviewed in (Dosemeci et al., 2002)], and in a study of 2,4-D and MCPA (Coble et al., 2005). Other PPE included chemically resistant boots or shoes, chemically resistant aprons, disposable coveralls, cartridge respirator/gas masks, and/or goggles used more than half the time.

Three hygiene questions sought information on whether respondents usually bathed or showered after mixing or applying pesticides and before continuing with other farm activities, whether they changed their clothes after using pesticides, and whether they consistently washed concentrated pesticides off their skin after exposure.

2.3. Data analysis

All analyses were performed in SAS (version 9.2, SAS Institute, Cary, NC). Participant characteristics are reported for the 306 subjects in our study population who completed the FAME PPE survey. We used logistic regression to assess whether sex, education, smoking status, age, state, or applicator status (pesticide applicator or spouse) differed between those included in the present analysis and the remainder of the FAME population. We used chi square tests to examine participant characteristics by case status. We examined the associations between PD and pesticides, PPE, and hygiene practices using unconditional logistic regression and obtained stratum-specific estimates from interaction models via the estimate statement in PROC GENMOD.

2.3.1. Covariates

Information on covariates was obtained during FAME interviews. Frequency-matching variables state, sex, and reference age were always

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